REMARKS/ARGUMENTS

Claims 66-71, 73-75 and 77-85 and 87-98 are active in this case.

Support for the definition of T-cells and their use in the claimed method is found on page 6, lines 1-6; page 7, lines 10-22; and page 9, 2nd and 3rd paragraphs. Support for newly added Claims 87-98 also finds support in these sections of the specification as well as page 11, 2nd and 3rd paragraphs; and page 22, line 9 to page 23, line. 9.

No new matter is believed to have been added by the amendments.

As the claims have been amended as well as new claims added in this response after final rejection, a Request for Continued Examination is also being filed with this paper.

Applicants thank the Examiner for the courtesy of discussing this case with their undersigned representative on June 13, 2007. During this discussion, the enablement and prior art rejections were discussed. Further details on this discussion are reflected in the remarks below.

The rejection under 35 USC 112, first paragraph based on the allegation that the claims are not enabled is respectfully traversed.

As has been discussed previously, the invention is based on the discovery that culturing cells in the manner defined in the claims allows one to obtain cells that have significant capabilities in proliferating *ex vivo* and the cells obtained also have higher biological function, i.e., are more potent cells (referring to pages 5-6 of the specification). Because the cells which are cultured according to the conditions claimed are more potent, these cells have a far greater capacity to be used in therapeutic applications wherever such cells are used. In other words, there is a body of evidence that is known in the art of using T-cells for therapeutic purposes. The inventors have discovered a way to make these cells better and more potent for such therapeutic applications.

The claims of this application are directed to methods of obtaining human T cells with enhanced replicative potential and their subsequent use in providing immunotherapy in a patient. Those cells are cultured under certain conditions as defined in the claims. As discussed in the specification, an advantage of the present invention is the discovery that culturing cells, including T-cells, one can obtain a population of cells with enhanced replicative and/or biological function (such as enhanced cytolysis and secretion of cytokines—see Claim 94) making these cells particularly useful for therapeutic applications such as immunotherapy.

As discussed in the specification on page 10:

> Static culture conditions for the comparative purposes are conditions employing the same medium, same starting cell inoculum source except grown without frequent medium exchange. For example, the T-cell concentration in a conventional low density culture is allowed to reach a maximum of 2-4 x 10^6 cells/ml during cell growth with time. After growth to this maximum density, the cell concentration is reduced to 5 x 10^5 cells/ml and the cells are allowed to grow again to 2-4 x 10^6 cells/ml. This cycle of growth to maximum cell density followed by a reduction of 5 x 10^5 cells/ml is repeated throughout the entire culture period.
>
> In contrast, in the method of the present invention for culturing T-cells, the cell density is not substantially reduced or adjusted at any time during the culture period. Thus, T-cells grow to maximum cell densities of 12-40 x 10^6 cells/ml under conditions of culture medium replacement.

Moreover, Example 1 (pages 23-24) demonstrates *ex vivo* expansion of T-cells under medium replacement conditions representative of those being claimed. Example 2 also demonstrates the power of culturing T-cells under medium replacement conditions. That such cultured T-cells can be used in immune therapies, such as adoptive immunotherapy etc, is supported by the knowledge in the field, e.g., as cited on pages 22-23 of the specification

demonstrating the usefulness of T-cells in such therapy protocols. Copies of the references cited are attached in further support of the claimed method.

Accordingly, it should be apparent that the specification as originally filed coupled with the knowledge available in the art at that time, enables the culturing and generation of human T-cells and their use as now claimed.

Withdrawal of this rejection is requested.

The rejection based on the combination of US '126 and US '994 under 35 USC 103(a) is not applicable to the claims as presented herein. US '126 primarily focuses on the culturing and use of dendritic cells. Indeed, dendritic cells are a special type of antigen-presenting cell (APC) that activates T lymphocytes as conventionally known in the field and therefore differ from T-cells as defined in the claims of this application.

US '994 describes culturing stem cell and progenitor cells obtained from bone marrow (see paragraph bridging cols. 4-5 and col. 5, lines 59-66) and their application for the use in bone marrow transplantation (see col. 2, lines 51-53). There is no indication or disclosure in US '994 to culture human T-cells nor that such cultured T-cells can be used in the manner as is claimed in the present application.

Therefore, US '994 in combination with US '126 fail to describe that by culturing the cells in accordance with the method claimed, one would want to or could provide immunotherapy to a patient with cultured T-cells as claimed.

Accordingly, withdrawal of this rejection is requested.

Finally, a Notice of Allowance indicating all claims have been allowed is requested.

Respectfully submitted,

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